

such as the Drosophila paired protein; proteins with domains whose structures depend on metal ion chelation such as Cys2His2 (SEQ ID NO: 4) zinc fingers found in TFIIIA, Zn2(Cys)6 (SEQ ID NO: 5) cluster such as those found in yeast Gal4, the Cys3 His (SEQ ID NO: 6) box found in retroviral nucleocapsid proteins, and the Zn2(Cys)8 (SEQ ID NO: 7) clusters found in nuclear hormone receptor-type proteins; the phage P22 Arc and Mnt repressors (see Knight et al. (1989) J. Biol. Chem. 264: 3639-3642 and Bowie & Sauer (1989) J. Biol. Chem. 264: 7596-7602. RNA binding proteins are reviewed by Burd & Dreyfuss (1994) Science 265: 615-621, and include HIV Tat and Rev.

In accordance with 37 CFR § 1.121 a marked up version of the above-amended paragraph(s) illustrating the changes introduced by the forgoing amendment(s) is provided in Appendix C.

In the Claims:

Cancel claims 24-50 without prejudice.

Amend the claims by substituting the following claims for the corresponding previously pending claims of the same number(s):

1. (Amended) A method for producing and screening a cell-specific binding molecule for an ability to increase uptake or specificity of a genetic vaccine for a target cell, the method comprising:

creating a library of recombinant polynucleotides by recombining at least one nucleic acid that encodes a polypeptide that comprises a nucleic acid binding domain and at least one nucleic acid that encodes a polypeptide that comprises a cell-specific binding domain; and

screening at least one member of the library for a recombinant polynucleotide that encodes a binding molecule that can bind to a nucleic acid and to a cell-specific receptor.

sub D' 2. (Amended) A method for producing and screening a recombinant cell-specific binding moiety for an ability to increase uptake or specificity of a genetic vaccine for a target cell, the method comprising:

(1) recombining at least first and second forms of at least one nucleic acid which comprises a polynucleotide that encodes a nucleic acid binding domain and at least first and second forms of at least one nucleic acid which comprises a polynucleotide

that encodes a cell-specific ligand that specifically binds to a protein on the surface of a cell of interest, wherein the first and second forms differ from each other in two or more nucleotides, to produce a library of recombinant binding moiety-encoding nucleic acids;

(2) introducing into one or more host cells one or more members of a library of vectors, each of which comprises: a) a binding site specific for the nucleic acid binding domain and b) a member of the library of recombinant binding moiety-encoding nucleic acids, wherein the encoded recombinant binding moiety is expressed;

(3) binding the expressed recombinant binding moiety to a vector comprising the binding site to form a vector-binding moiety complex;

(4) contacting the vector-binding moiety complex with a target cell of interest; and

(5) determining if one or more target cells contain a vector, and recovering the recombinant cell-specific binding moiety nucleic acid from any such target cells.

3. (Amended) The method of claim 2, wherein the method further comprises:

(6) recombining at least one recombinant binding moiety-encoding nucleic acid of (5) with a further form of the polynucleotide that encodes a nucleic acid binding domain and/or a further form of the polynucleotide that encodes a cell-specific ligand, which are the same or different from the first and second forms, to produce a further library of recombinant binding moiety-encoding nucleic acids;

(7) introducing into one or more host cells one or more members of a library of vectors, each of which comprises: a) a binding site specific for the nucleic acid binding domain and b) a member of the further library of recombinant binding moiety-encoding nucleic acids, wherein the encoded recombinant binding moiety is expressed;

(8) binding the expressed recombinant binding moiety to a vector comprising the binding site to form a vector-binding moiety complex;

(9) contacting the vector-binding moiety complex with a target cell of interest and determining if one or more target cells contain a vector;

(10) recovering the recombinant binding moiety nucleic acid from any such target cells; and

(11) repeating (6) through (10) to screen for a cell-specific binding moiety useful for increasing uptake or specificity of a genetic vaccine vector for a target cell.

4. (Amended) The method of claim 2, wherein the method comprises screening for one or more cell-specific binding moieties that increase uptake of a genetic vaccine vector by the target cells.

5. (Amended) The method of claim 2, wherein the nucleic acid binding domain is a DNA binding domain derived from a protein selected from the group consisting of a transcriptional regulator, a polypeptide involved in DNA replication or recombination, a repressor, a histone, a protamine, an E. coli CAP protein, myc, a protein having a leucine zipper, a protein having a DNA binding basic domain, a protein having a POU domain, a protein having a zinc finger, and a protein having a Cys3His (SEQ ID NO:6) box.

7. (Amended) The method of claim 2, wherein the target cell of interest is selected from the group consisting of muscle cells, monocytes, dendritic cells, B cells, T cells, Langerhans cells, keratinocytes, M-cells, liver cells and epithelial cells.

8. (Amended) The method of claim 7, wherein the target cell of interest is a professional antigen presenting cell.

10. (Amended) The method of claim 8, wherein the cell-specific ligand comprises a polypeptide derived from a protein selected from the group consisting of CD2, CD28, CTLA-4, CD40 ligand, fibrinogen, ICAM-1, Fc portion of immunoglobulin G, and a bacterial enterotoxin, or a subunit thereof.

12. (Amended) The method of claim 2, wherein target cells that contain the vector are identified by selecting for expression of a selectable marker contained in the vector.

13. (Amended) The method of claim 2, wherein each recombinant binding moiety-encoding nucleic acid comprises a genetic vaccine vector.

sub D² 14. (Amended) A cell-specific recombinant binding moiety produced by expressing in a host cell a recombinant binding moiety-encoding nucleic acid obtained by the method of claim 2, wherein the nucleic acid binding domain is a DNA binding domain derived from a protein selected from the group consisting of a transcriptional regulator, a polypeptide involved in DNA replication or recombination, a repressor, a histone, a protamine, an E. coli CAP protein, myc, a protein having a leucine zipper, a protein having a DNA binding basic domain, a protein having a POU domain, a protein having a zinc finger, and a protein having a Cys3His (SEQ ID NO:6) box or the nucleic acid binding domain is an RNA binding domain derived from a protein selected from the group consisting of HIV tat and HIV rev.

15. (Amended) A composition for eliciting an immune response that comprises a cell-specific recombinant binding moiety of claim 14.

sub D 3 16. (Amended) A composition for eliciting an immune response that comprises a recombinant binding moiety-encoding nucleic acid obtained by the method of claim 2, wherein the nucleic acid binding domain is a DNA binding domain derived from a protein selected from the group consisting of a transcriptional regulator, a polypeptide involved in DNA replication or recombination, a repressor, a histone, a protamine, an E. coli CAP protein, myc, a protein having a leucine zipper, a protein having a DNA binding basic domain, a protein having a POU domain, a protein having a zinc finger, and a protein having a Cys3His (SEQ ID NO:6) box or the nucleic acid binding domain is an RNA binding domain derived from a protein selected from the group consisting of HIV tat and HIV rev.

B3 17. (Amended) A composition for eliciting an immune response that comprises:

- a) a recombinant binding moiety that comprises a nucleic acid binding domain and a cell-specific ligand, and
- b) a polynucleotide sequence that is capable of expressing an antigen comprises a binding site, wherein the nucleic acid binding domain is capable of specifically binding to the binding site.

18. (Twice Amended) A method for producing and screening a recombinant cell-specific binding moiety for an ability to increase uptake, efficacy, or specificity of a vaccine or antigen for a target cell, the method comprising:

- (1) recombining at least first and second forms of at least one nucleic acid that comprises a polynucleotide which encodes a binding moiety of an enterotoxin, wherein the first and second forms differ from each other in two or more nucleotides, to produce a library of recombinant nucleic acids;
- (2) introducing one or more members of a library of vectors, each of which comprises a member of the library of recombinant nucleic acids, into one or more host cells, wherein the member of the library of recombinant nucleic acids is expressed to form a recombinant cell-specific binding moiety polypeptide;
- (3) contacting the recombinant cell-specific binding moiety polypeptide with a cell surface receptor of a target cell; and
- (4) determining if the recombinant cell-specific binding moiety polypeptide exhibits enhanced ability to bind to the target cell.

B³ 19. (Amended) The method of claim 18, wherein the cell surface receptor is present on the surface of a target cell during said contacting.

B⁴ 22. (Amended) A method for producing a composition for eliciting an immune response, the method comprising coating a polynucleotide that is capable of expressing an antigen with a recombinant cell-specific binding moiety produced by the method of claim 18.

23. (Amended) The method of claim 18, wherein the recombinant cell-specific binding moiety polypeptide is expressed as a fusion protein on the surface of a replicable genetic package.

sub D⁴ 51. (Amended) A method for producing and screening a recombinant cell-specific binding moiety polypeptide for an ability to increase uptake, efficacy, or specificity of a vaccine antigen for a target cell, the method comprising:

(1) recombining at least first and second forms of at least one nucleic acid that comprises a polynucleotide which encodes a cell-specific binding moiety, wherein the first and second forms differ from each other in two or more nucleotides, to produce a library of recombinant nucleic acids;

B⁵ (2) introducing one or more members of a library of vectors, each of which comprises a member of the library of recombinant nucleic acids, into one or more host cells, wherein the member of the library of recombinant nucleic acids is expressed to form a recombinant cell-specific binding moiety polypeptide;

(3) contacting the recombinant cell-specific binding moiety polypeptide with a cell surface receptor of a target cell;

(4) determining if the recombinant cell-specific binding moiety polypeptide exhibits enhanced ability to bind to the target cell; and

(5) fusing or linking the recombinant cell-specific binding moiety polypeptide to the vaccine antigen or coating the vaccine antigen with the recombinant cell-specific binding moiety polypeptide.

sub D⁵ 53. (Amended) The method of claim 51, wherein the recombinant cell-specific binding moiety polypeptide is fused or linked to the vaccine antigen.

B⁶ 54. (Amended) The method of claim 51, wherein the target cell is selected from the group consisting of muscle cells, monocytes, dendritic cells, B cells, T cells, Langerhans cells, keratinocytes, M-cells, liver cells and epithelial cells.

55. (Amended) The method of claim 51, wherein the cell surface receptor is present on the surface of a target cell during said contacting.

B6

56. (Amended) The method of claim 51, wherein the cell-specific binding moiety comprises a polypeptide derived from a protein selected from the group consisting of selected from the group consisting of CD2, CD28, CTLA-4, CD40, and ligands thereof; fibrinogen; factor X; ICAM-1; β -glycan; Fc portion of immunoglobulin G; and a bacterial enterotoxin, or a subunit thereof.

sub D6

57. (Amended) A method for producing a composition for eliciting an immune response, said method comprising coating an antigen with a recombinant cell-specific binding moiety polypeptide produced by the method of claim 51.

58. (Amended) A composition for eliciting an immune response comprising an antigen and a recombinant cell-specific binding moiety polypeptide, wherein the composition is produced by the method of claim 51.

Add the following claims:

B7

59. The method of claim 2, wherein the binding site of each vector is derived from a binding site present in at least one form of at least one nucleic acid of (1).

60. The method of claim 2, wherein the binding site is joined to the member of the library of recombinant binding moiety-encoding nucleic acids after said recombining.

61. The method of claim 2, wherein the vector-binding moiety complex forms inside the host cell and, prior to the contacting of (4), the host cell is lysed under conditions that do not disrupt the vector-binding moiety complex.

62. The method of claim 3, wherein the vector-binding moiety complex of (8) forms inside the host cell and, prior to the contacting of (9), the host cell is lysed under conditions that do not disrupt the vector-binding moiety complex.

63. The method of claim 2, wherein the cell-specific ligand comprises a polypeptide derived from a protein selected from the group consisting of CD2, CD28, CTLA-4, CD40, and ligands thereof; fibrinogen; factor X; ICAM-1; β -glycan; Fc portion of immunoglobulin G; and a bacterial enterotoxin, or a subunit thereof.

64. The method of claim 51, wherein the vaccine antigen is coated with the recombinant cell-specific binding moiety polypeptide.

These amendments are made without prejudice and are not to be construed as abandonment of the previously claimed subject matter or agreement with the Examiner's